

REMARKS

Claims 28-60 are pending. No new matter has been added by way of the above amendments. For example, claim 28 corresponds to previously pending claims 15 and 21. Claims 29, 38 and 49 are supported by the present specification at page 9, line 1 and page 11, lines 19-21. New claims 30-34 correspond to previously pending claims 16-20 and new claims 35, 36 and 52-54 correspond to the subject matter of previously pending claims 23 and 24. New claim 37 corresponds to previously pending claims 1 and 21 and new claims 38-42 correspond to previously pending claims 2-5. New claim 43 is supported by previously pending claim 20 and new claims 44-47 and 55-57 correspond to the subject matter of previously pending claims 6 and 8-10. Lastly, new claims 48, 50, 51 and 58-60 correspond to the subject matter of previously pending claims 11, 13 and 14. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issues Under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 1-24 and 26 (which is presumably exclusive of claims 7, 12 and 22, withdrawn from

consideration) for the reasons recited at pages 2-4 of the outstanding Office Action. The Examiner asserts that the specification provides sufficient written description for a method of using the conjugate or complex to deliver a nucleic acid across the cell membrane to a location within a cell, but does not allegedly provide description of a genus of "direction thereof". Applicants respectfully traverse this rejection.

First, Applicants respectfully submit that the newly submitted claims require the specific synthetic transport entity, for instance as recited in claim 28. Second, Applicants respectfully submit that the recitation of "direction thereof" has been removed from the claims. Accordingly, Applicants respectfully submit that the currently pending claims are fully supported by the present specification in such a way that one of ordinary skill in the art would have understood that the inventors, at the time the application was filed, had possession of the claimed invention. Reconsideration and withdrawal of this rejection are respectfully requested.

The Examiner has also rejected claims 1-24 and 26 (presumably exclusive of claims 7, 12 and 22, withdrawn from consideration) for the reasons recited at pages 4-6 of the outstanding Office Action. The Examiner asserts that the present specification, while being enabling for a method of delivering a nucleic acid into a target cell comprising the step

of using the recited complex or conjugate to deliver a nucleic acid across a cell membrane of the target cell; and a method of delivering a nucleic acid across the nuclear membrane of a target cell comprising the step of delivering the recited complex or conjugate into the cell, wherein the FE comprises a NLS, does not allegedly provide enablement for embodiments embracing the delivery of a nucleic acid across or from any "direction" to a specific location within or on a cell or for any targeted delivery of any specific location other than the nucleus of any target cell. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the presently pending claims are fully enabled by the present specification. Applicants direct the Examiner's attention to independent claim 28 which recites the specific structure of the synthetic transport entity. Moreover, Applicants note that the language relating to "direction thereof" has been removed from the claims. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Issues Under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1, 10, 11 and 13 (Applicants believe that the recitation of claim 13 is an error

and should embrace claims 15 and 24 instead). Regardless, Applicants respectfully traverse these rejections.

First, the Examiner has rejected claims 1 and 10 for the recitation of "each as in HIV protein". Applicants respectfully traverse and submit that this language has been removed from the claims. Reconsideration and withdrawal thereof are respectfully requested.

Second, the Examiner has rejected claims 1, 10, 15 and 24 for reciting "e.g.,". Applicants respectfully traverse and submit that this language has been removed from the claims and the relevant subject matter placed into suitable dependent claims. Reconsideration and withdrawal thereof are respectfully requested.

Third, the Examiner has rejected various claims for the recitation of "such as". Applicants respectfully traverse and submit that this language has been removed from the claims and the relevant subject matter placed into suitable dependent claims. Reconsideration and withdrawal thereof are respectfully requested.

Fourth and lastly, the Examiner has rejected claim 26 for the recitation of a use without any specific step. Applicants traverse and submit that this language has been removed from the presently pending claims. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. §101

The Examiner has rejected claim 26 under 35 U.S.C. §101 asserting that the recitation of a use without setting forth any steps is improper. Applicants traverse and submit that the subject matter relating to claim 26 is no longer present in the currently pending claims. Reconsideration and withdrawal thereof are respectfully requested.

Objections to the Claims

The Examiner has objected to the dependent claims asserting that the recitation of "A" at the beginning of the claims should be replaced with "The". Applicants traverse and submit that all currently pending dependent claims have adopted this format. Reconsideration and withdrawal of this objection is requested.

Issues Under 35 U.S.C. §102(e)/103(a)

The Examiner has rejected claims 1-6, 8-11, 13-21, 23, 24 and 26 under 35 U.S.C. §102(e), as being anticipated by, or in the alternative under 35 U.S.C. §103(a) as being obvious over Felgner et al., USP 6,165,720 (hereinafter referred to as Felgner '720). Applicants respectfully traverse.

Distinctions Between the Present Invention and Felgner '720

Felgner '720 discloses a nuclear acid delivery complex, which differs from the one claimed in the present application. In the present claims, the simultaneous use of more than one single functional element (FE) is described. Felgner '720 fails to suggest or disclose the simultaneous use of multiple ligands. The reasons for this may be found in the technology developed by Felgner '720.

Felgner '720 uses PNA clamps, also referred to as bis-PNA. The DNA target sequence for such a clamp is made up of an AG-repeat as illustrated in Fig. 3A and as further exemplified in Example 1 (col. 12/13), Example 3 (col. 13/14) and in Example 22 (col. 26-28) (all referring to Felgner '720); in Example 22 the AG-opposite strand TC-repeat is presented.

In one embodiment of the present invention the PNA sequence denoted (GCG CTC GGC CCT TTC) is a mixed chimera, which can easily be altered. Thus, using a vector with two different BE (binding element) target sequences, two different BEs can be used, each carrying a unique FE (functional element). Attached is an experiment using the Human Immunodeficiency Virus 1 (HIV-1) TAT peptide and a novel branched peptide, each linked to a specific BE. The use of both FE-BE complexes gives an uptake of the vector that is greater than the sum of the uptake of vector when each FE-BE is used separately.

Accordingly, due to the lack of disclosure in Felgner '720 of more than one functional element, no anticipation, nor obviousness exists based upon Felgner '720. Moreover, as shown in the attached experimental data, when more than one functional element-binding element complex is utilized, there exists a level of uptake of the vector which is greater than the sum of the uptake of the vector when these complexes are used separately. Such results are unexpectedly superior to the disclosure of the cited art, thus, any hypothetical *prima facie* case of obviousness is rebutted.

In view of the above, Applicants respectfully submit that the present claims define subject matter which is patentable over the prior art of record. Accordingly, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Initialed Form PTO-1449

On March 13, 2001, Applicants filed an Information Disclosure Statement including a Form PTO-1449 which listed five references. With the exception of one of these references (WO 93/19768), the references cited in this Form PTO-1449 were duplicated in the Information Disclosure Statement filed on June 13, 2001. The Examiner has returned an initialed copy of the June 13, 2001 Form PTO-1449. However, WO 93/19768 listed on the

Form PTO-1449 filed on March 13, 2001, has not yet been initialed by the Examiner. The Examiner is therefore respectfully requested to provide Applicants with an initialed copy of this Form PTO-1449 indicating that this reference has been considered.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No. 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

Applicants have attached hereto a marked up version of the claims to show the changes made for the Examiner's convenience.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1-27 have been cancelled.

Claims 28-60 have been added.